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Safety Assessment of Topical Formulation of Nicotinamide Gel (2%), (3%) and (4%) on Skin of Normal Healthy New Zealand White Albino Rabbits.

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ABSTRACT

Nicotinamide, a physiologically active form of niacin (nicotinic acid), in combination with zinc is being assessed in clinical studies for the treatment of inflammatory skin diseases such as acne vulgaris and bullous pemphigoid. Consequently the aim of the present study was to investigate the safety profile of Nicotinamide gel 2%, 3% and 4% (Apex Laboratories Private Limited, Chennai, India on skin of normal healthy New Zealand White Albino rabbits. The safety assessment was done for the single dose topical application of Nicotinamide 2%, 3% and 4% gel by the Draize skin test method in New Zealand White Albino rabbits. The topical application of Nicotinamide gel did not cause any erythema and edema in the skin of New Zealand White Albino rabbits like the control group. The primary irritation index was found to be zero which indicates the non-irritant nature of Nicotinamide 2%, 3% and 4% gel. Further, clinical evaluation has to be performed to precisely define the long term dermal safety of Nicotinamide gel 2%, 3% and 4% of human subjects.

Keywords: Nicotinamide gel, Safety, Dermal reactions, Draize skin test, Rabbit

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INTRODUCTION

The skin is often exposed, either intentionally or unintentionally, to medicinal or cosmetic products. It is clear that the potential for a particular product/ingredient to cause skin irritation or for a particular ingredient to cause skin corrosion needs to be carefully evaluated as part of the overall safety assessment process. It is generally assessed by the potential of a certain substance to cause erythema/eschar and/or edema after a single topical application on rabbit skin and based on the Draize score (OECD TG 404, 2002) [1].

Nicotinamide is one of the newly discovered vitamin-based components of cosmeceutical products. It is found to possess anti-inflammatory and anti-acne actions [2]. In the present study, the safety of single dose application of topical Nicotinamide 2%, 3% and 4% gel was assessed using Draize skin test in adult New Zealand White Albino rabbits.

MATERIALS AND METHODS

Animals

8 adult New Zealand White Albino rabbits of either sex weighing 1.0–1.5 kg were housed individually in polypropylene cages, maintained under standard conditions with temperature (22–24^0 C), 12-h light/12-h dark cycle and relative air humidity 40–60%. Rabbits had continuous access to norm caloric diet (Amrit Feeds Private Ltd., Pune, India) and to tap water. The animals were acclimatized to the laboratory conditions for one week before the start of the experiment. The animals were acclimatized to the laboratory conditions for one week before the start of the experiment. The experimental protocol was approved by the Institutional Animal Ethics Committee (IAEC/KMC/03/2014) and experiments were conducted according to the ethical norms approved by Ministry of Social Justices and Empowerment (Government of India), Committee for the Purpose of Control and Supervision on Experiments on Animals (CPCSEA) guidelines.

Drugs

Nicotinamide 2%, 3% and 4% gel were obtained from Apex Laboratories Private Limited, Chennai (India) as kind gift sample.

Experimental procedure

In the experiment a total of 8 adult New Zealand White Albino rabbits of either sex were used. The skin safety study was conducted on four groups of rabbits (2 per group) of either sex weighing 1.0 -1.5 kg. Approximately, 24 hours before initiation of the experiment, the back of the animals were clipped free of fur at four sites using an oster small animal clipper without any abrasions with an area of 6 cm^2. In each group, the skin of one rabbit was left intact and the skin of the other rabbit was abraded with a clipper head so as to penetrate the horny layer of the epidermis without causing bleeding. A 0.5 g quantity of sample of the Nicotinamide gel was weighed and then evenly applied to each site [2]. All the four sites were covered with a non-occlusive absorbent gauze patch and held in place with non-irritating tape then the patch were wrapped with semi-occlusive bandage for the duration of 4 hours. Rabbits were kept in restrainer for 4 hours. Following the 4 hours exposure period, the collars and wrappings were removed and any remaining test materials were removed with a wet disposable paper towel without altering the integrity of the epidermis [2]. All the animals were observed for dermal reactions at 1, 24, 48 and 72 hours following the removal of gauze patch, the test sites were examined for erythema and edema in accordance with Draize scoring criteria (Table 1).

Two rabbits of each group received the drugs as:

Group I– Control
Group II– Nicotinamide 2% gel
Group III– Nicotinamide 3% gel
Group IV– Nicotinamide 4% gel

Table 1: Draize Evaluation of Dermal Reactions:

Skin Reactions	Score
Erythema	
No erythema	0
Very slight erythema (barely perceptible)	1
Well defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness)	4
Edema	
No edema	0
Very slight edema (barely perceptible)	1
Slight edema(edges of area well defined by definite raising)	2
Moderate edema (raised approximately 1 mm)	3
Severe edema(raised more than 1 mm and extending beyond the area of exposure	4

The scores for erythema and edema were totaled for intact and abraded skin for all rabbits at 24 and 72 hours. The primary irritation index (PII) was calculated, based on the sum of the scored reactions divided by 24 (two scoring intervals) multiplied by two (test parameters) and further multiplied by two (rabbits).

Table 2: Evaluation of Primary Irritation Index (PII):

Index	Evaluation
0.00	No irritation
0.04-0.99	Irritation barely perceptible
1.00-1.99	Slight irritation
2.00-2.99	Mild irritation
3.00-5.99	Moderate irritation
6.00-8.00	Severe irritation

RESULTS

There was no erythema and edema observed during Draize skin test for dermal reactions in normal control and Nicotinamide gel (2%, 3% and 4%) treated rabbits. The primary irritation index (PII) was found to be 0.00 (No irritation) in all the rabbits used for Draize skin test for dermal reactions.

DISCUSSION

The Draize test is an acute toxicity test devised in 1944 by Food and Drug Administration (FDA) toxicologists John H. Draize and Jacob M. Spines. The present study demonstrated that the Nicotinamide gel 2%, 3% and 4% (Apex Laboratories Private Limited, Chennai, India) is found to be safe (no erythema and edema) during the Draize skin test in New Zealand White Albino rabbits. Many of the studies support the results of the present study. One of the clinical studies suggests the safety and efficacy of topical formulation of nicotinamide 4% in acne [3]. One of the pre-clinical studies suggests that skin sensitization tests of Niacinamide at 5% during induction and 20% during challenge were negative in guinea pigs [4]. Further, clinical evaluation has to be performed to precisely define the long term dermal safety of Nicotinamide gel 2%, 3% and 4% of human subjects.

REFERENCES

[1] Draize JH, Woodard G, Calvery HO. J Pharmacol Exp Thers 1944;82:377-390.
[2] Griffiths CEM. J Dermatol Treat 1995;6:S8-S10.
[3] Emanuele E, Bertona M, Altabas K, Altabas V, Alessandrini G. Cosm Invesl Dermatol 2012;5:33–7.
[4] Int J Toxicol 2005;24(suppl 5):1-31.